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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/781,182	02/12/2001	John N. Vournakis	7867-022-999	2779

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 08/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/781,182	Applicant(s) VOURNAKIS ET AL.	
	Examiner Patrick T. Lewis	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-5, 11-17, 24-28, 32-34, and 36-38 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for achieving at least a transient, localized, modulation of vascular structure and/or function; a method of treating a patient having a vascular disorder; and compositions comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers wherein the polymer comprises 50 to about 150,000 monosaccharide units, does not reasonably provide enablement for a method for achieving at least a transient, localized, modulation of vascular structure and/or function; a method of treating a patient having a vascular disorder; and compositions comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers of any molecular weight or size. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims without undue experimentation.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the

application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors include, but are not limited to:

1. The breadth of the claims,
2. The nature of the invention,
3. The state of the prior art,
4. The level of one of ordinary skill,
5. The level of predictability in the art,
6. The amount of direction provided by the inventor,
7. The existence of working examples, and
8. The quantity of experimentation needed to make and/or use the invention based on the content of the disclosure.

Claims 1-5, 11-17, and 26-28 are drawn to a method for achieving at least a transient, localized, modulation of vascular structure and/or function comprising topically administering to a patient in need of said modulation, a material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, wherein said administering induces at least a transient, localized physiological response selected from the group consisting of stimulation of endothelin-1 release, vasoconstriction, and reduction in blood flow out of a breached vessel, whereby the patient experiences at least a transient, localized modulation of vascular structure and/or function. Claims 24-25 and 32-34 are drawn to a method for treating a patient having a vascular disorder comprising topically administering to a patient in need of such treatment, a material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, wherein said administering induces at least a transient, localized physiological response selected from the group consisting of stimulation of endothelin-1 release, vasoconstriction, and reduction in blood flow out of a breached vessel, whereby the patient experiences at

least a transient, localized modulation of vascular structure and/or function, whereby said administering ameliorates said vascular disorder. Claims 36-38 are drawn to the pharmaceutical composition of claim 34, wherein said polymers are substantially free of protein.

The examiner notes that US 6,063,911 discloses methods and compositions comprising at least one endothelin antagonist, preferably in combination with a poly-β-1→4 N-acetylglucosamine polysaccharide matrix, for use in the treatment of cancer and other proliferative diseases.

The skilled artisan in this field is that of an MD for chemotherapeutic administration and/or a PhD skilled in the development of chemotherapeutics.

The examiner acknowledges the probability and predictability that some poly-β-1→4 N-acetylglucosamine polymers may have applicability, specifically the poly-β-1→4 N-acetylglucosamine polymers comprising about 50 to about 150,000 N-acetylglucosamine monosaccharides. To contend that applicant has envisioned and prepared poly-β-1→4 N-acetylglucosamine polymers outside this range useful for achieving at least a transient, localized, modulation of vascular structure and/or function comprising topically administering to a patient in need of said modulation or for treating a patient having a vascular disorder comprising topically administering to a patient in need of such treatment, wherein said administering induces at least a transient, localized physiological response is to extrapolate beyond that which has been set forth in the instantly claimed disclosure.

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to enable the treatment vascular disorders or the achievement of at least a transient, localized, modulation of vascular structure and/or function comprising topically administering to a patient in need of said modulation, a material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, wherein said administering induces at least a transient, localized physiological response.

The working examples in the instant specification are limited to the use of semi-crystalline poly-β-1→4 N-acetylglucosamine polymers wherein the polymer comprises 50 to about 150,000 monosaccharide units.

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the use semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, wherein the polymer is outside the range of about 50 to about 150,000 N-acetylglucosamine monosaccharides. Applicant's disclosure is seen to only enable the use of polymers within this range.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. In claims 1 and 24, it is unclear what quantitative measure applicants intend to use to obtain a "sufficient amount", when what the amount is intended to be "sufficient"

to achieve is unclear, ambiguous and indefinite. The examiner suggests deleting the term "administering induces" (claim 1, line 5; claim 24, line 5) and inserting the term "sufficient amount achieves" therefor.

6. Regarding claims 18-23, 29-31, and 35, the term "non-barrier-forming" is unclear. Applicant discloses that the "non-barrier-forming" material may be in the form of a gel, sponge, film, membrane, foam, spray, emulsion, suspension, or solution, all of which are seen be a "barrier" depending on how the term is defined.

7. Claims 36-38 recite the limitation "pharmaceutical composition of claim 34" in the first line of each claim. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 1-17, 24-28, and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vournakis et al. US 5,635,493 (Vournakis) in view of Barton et al. *Curr. Opin. Nephrol. Hypertens.* (**1999**), vol. 8, pages 549-556 (Barton) and Pearson *Lupus* (**2000**), vol. 9, pages 183-188 (Pearson).

Claims 1-17 and 26-28 are drawn to a method for achieving at least a transient, localized, modulation of vascular structure and/or function comprising topically administering to a patient in need of said modulation, a material comprising semi-crystalline poly-β-1$^{\rightarrow}$4 N-acetylglucosamine polymers. Claims 24-25 and 32-34 are drawn to a method for treating a patient having a vascular disorder comprising topically administering to a patient in need of such treatment, a material comprising semi-crystalline poly-β-1$^{\rightarrow}$4 N-acetylglucosamine polymers.

Vournakis teaches methods and compositions comprising poly-β-1$^{\rightarrow}$4 N-acetylglucosamine (p-GlcNAc) materials (column 36, lines 45-52). The materials may

be used to promote hemostasis and wound healing (column 35, lines 40-52). The p-GlcNAc materials may be applied directly to bleeding surfaces thereby arresting bleeding by providing a mechanical matrix that promotes clotting (column 35, lines 46-48). The p-GlcNAc material comprises a crystalline polymer of high molecular weight ranging from 800,000 daltons to 30 million Daltons corresponding to a polymer having about 4,000 to about 150,000 N-acetylglucosamine monosaccharides (column 9, lines 16-25; column 13, lines 53-57). The p-GlcNAc is free of detectable protein contaminants, is substantially free of other organic contaminants such as free amino acids, and is substantially free of inorganic contaminants (column 9, lines 36-56). One or more of the monosaccharide units of the p-GlcNAc may be deacetylated with 25% to 75% remaining acetylated (column 15, lines 58-67; column 16, lines 1-8). The compositions may be in the form of mats, strings, microspheres, microbeads, membranes, fibers, powders, sponges, gels, and pharmaceutical formulations such as pills, tablets, and capsules (column 24, lines 36-44).

Vournakis differs from the instantly claimed invention in that Vournakis does not teach the compositions causing endothelin-1 release or vasoconstriction but rather reduction in the blood flow out of a breached vessel; Vournakis does not teach p-GlcNAc as being semi-crystalline; and Vournakis does not teach that the extent of the transient, localized modulation of vascular structure and/or function is proportional to the amount of p-GlcNAc administered. The deficiencies are, however, addressed by Pearson.

Barton teaches that the endothelin system has been implicated in the pathogenesis of arterial hypertension and renal disorders (page 549, column 1). Barton also teaches that endothelin-1 is the predominant isoform of the endothelin peptide family and regulates vasoconstriction and cell proliferation is tissues both within and outside the cardiovascular system. Pearson teaches that normal endothelial cell function is critical for all aspects of vascular homeostasis (page 183, column 1). Pearson further teaches that the active metabolism of these cells is necessary for the continuous adjustment of vascular tone, and hence the control of blood pressure; for the physiological regulation of leukocyte traffic from blood tissues; and for the maintenance of an antithrombotic and anticoagulant balance in flowing blood (page 183, column 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the prior art to arrive at the instantly claimed invention. It would have been obvious to one of ordinary skill in the art at the time of the invention that the method described by Vournakis would also induce the release of endothelin-1 and vasoconstriction since Vournakis teaches that the GlcNAc materials may be used to promote hemostasis and wound healing, and the prior art teaches that normal endothelial cell function is critical for all aspects of vascular homeostasis. It would have also been obvious to the skilled artisan that the more barrier-forming composition applied to a wound or breached blood vessel, the more bleeding would be reduced. The GlcNAc of instantly the claimed invention is described as being highly pure and semi-crystalline while the GlcNAc of Vournakis is described as being crystalline. In the absence of unexpected results, the degree of crystallinity is seen to

be a measure of purity rather than a structural limitation and may thus be used interchangeably. One would have been motivated to do so in order to treat skin wounds and reduce wrinkles.

12. Claims 18-23, 29-31, and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vournakis et al. US 5,635,493 (Vournakis).

Claims 18-23 and 29-31 are drawn to a biodegradable, non-barrier-forming material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers comprising about 50 to about 150,000 N-acetylglucosamine monosaccharides. Claim 35 is drawn to a pharmaceutical composition comprising a therapeutically effective amount of a biodegradable, non-barrier-forming material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers comprising about 50 to about 150,000 N-acetylglucosamine monosaccharides. Claims 36-38 are drawn to a pharmaceutical composition comprising a material comprising semi-crystalline poly-β-1→4 N-acetylglucosamine polymers, wherein said polymers are substantially free of inorganic contaminants.

Vournakis teaches methods and compositions comprising poly-β-1→4 N-acetylglucosamine (p-GlcNAc) materials (column 36, lines 45-52). The p-GlcNAc material comprises a crystalline polymer of high molecular weight ranging from 800,000 daltons to 30 million Daltons corresponding to a polymer having about 4,000 to about 150,000 N-acetylglucosamine monosaccharides (column 9, lines 16-25; column 13, lines 53-57). The p-GlcNAc is free of detectable protein contaminants, is substantially free of other organic contaminants such as free amino acids, and is substantially free of

inorganic contaminants (column 9, lines 36-56). One or more of the monosaccharide units of the p-GlcNAc may be deacetylated with 25% to 75% remaining acetylated (column 15, lines 58-67; column 16, lines 1-8). The compositions may be in the form of mats, strings, microspheres, microbeads, membranes, fibers, powders, sponges, gels, and pharmaceutical formulations such as pills, tablets, and capsules (column 24, lines 36-44).

Vournakis and instantly claimed invention differ in that instantly claimed invention is describes as being non-barrier-forming and semi-crystalline while Vournakis is described as being crystalline and barrier-forming.

It would have been obvious to one of ordinary skill in the art at the time of the invention to make compositions comprising poly-β-1→4 N-acetylglucosamine (p-GlcNAc) materials based on the teachings of Vournakis. The non-barrier-forming materials/compositions of the instantly claimed invention and the barrier-forming materials/compositions described by Vournakis are seen to be identical being that both are comprised of poly-β-1→4 N-acetylglucosamine and may be in the same form (i.e. gel, sponge, or film). The GlcNAc of instantly the claimed invention is described as being highly pure and semi-crystalline while the GlcNAc of Vournakis is described as being crystalline. In the absence of unexpected results, the degree of crystallinity is seen to be a measure of purity rather than a structural limitation and may thus be used interchangeably. The instantly claimed invention is thus prima facie obvious.

Conclusions

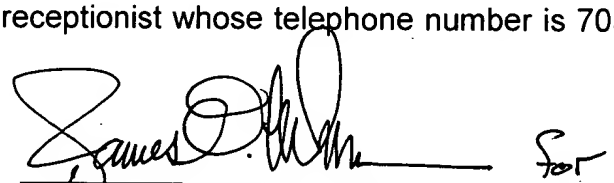
13. Claims 1-38 are pending. Claims 1-38 are rejected. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 703-305-4043. The examiner can normally be reached on M-F 8:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



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